

REMARKS

Claims 1-21 are pending in the application. Claims 1-21 are amended herein for clarity to more particularly define the invention. In addition, new claim 22 is added herein. Support for these amendments and the new claim is found in the language of the original claims and throughout the specification. No new matter is added by these amendments and the new claim and their entry is respectfully requested. In light of these amendments, the new claim and the following remarks, applicants respectfully request reconsideration of this application and allowance of the pending claims to issue.

I. Rejections under 35 U.S.C. §103 (a)

A. The Office Action states that claims 1-4, 11-14, and 16-18 are rejected under 35 U.S.C. §103 for allegedly being unpatentable over Laue (U.S. Patent No. 73734883) in view of Lowe et al. (Nucleic Acids Res. 18:1757-1761 (1990)). The Office Action states that Laue discloses forward primers, reverse primers and probes for the detection of SARS virus. Specifically, the Office Action alleges that SEQ ID NO:1 of Laue comprises instant SEQ ID NO:1 and instant SEQ ID NO:2. The Office Action further alleges that one of ordinary skill in the art would have been motivated to construct a pair of oligonucleotides with instant SEQ ID NOs:1 and 2 for amplifying a target sequence of the genome of SARS coronavirus with a reasonable expectation of success because Laue discloses a method of detecting SARS with a pair of primers and a known sequence and Lowe et al. discloses a computer program for selecting primers for PCR from a known sequence. On this basis, the Office Action concludes that it would have been *prima facie* obvious to construct a pair of oligonucleotides from within the instant SEQ ID NOs: 1 and 2 for amplifying a target sequence of the genome of SARS coronavirus as claimed. Applicants respectfully traverse this rejection.

As stated in the Examination Guidelines for Determining Obviousness, "the Supreme Court reaffirmed the familiar framework for determining obviousness as set forth in *Graham v. John Deere Co.*..." (Examination Guidelines for Determining Obviousness Under 35 U.S.C. 103 in View of the Supreme Court Decision in *KSR International Co. v. Teleflex Inc.* Federal Register Vol. 72, No. 195, 57526-57535, 57526). Hence, and as long established under that

framework, to establish a *prima facie* case of obviousness, three requirements must be satisfied. First, the prior art relied upon, coupled with the knowledge generally available in the art at the time of the invention, must contain some **suggestion or incentive that would have motivated** the skilled artisan to modify a reference or to combine references. *In re Oetiker*, 24 U.S.P.Q.2d 1443, 1446 (Fed. Cir. 1992); *In re Fine*, 837 F.2d at 1074; *In re Skinner*, 2 U.S.P.Q.2d 1788, 1790 (Bd. Pat. App. & Int. 1986). Second, the proposed modification or combination of the prior art must have a **reasonable expectation of success**, determined from the vantage point of the skilled artisan at the time the invention was made. *See Amgen, Inc. v. Chugai Pharm. Co.*, 927 F.2d 1200, 1209, 18 U.S.P.Q.2d 1016, 1023 (Fed. Cir. 1991). Third, the prior art reference or combination of references **must teach or suggest all of the limitations of the claims**. *See In re Wilson* 424 F.2d 1382, 1385, 165 U.S.P.Q. 494, 496 (CCPA 1970) ("All words in a claim must be considered in judging the patentability of that claim against the prior art"). Furthermore, as stated in *KSR Int'l Co. v. Teleflex In*, "[a] patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art." *KSR Int'l Co. v. Teleflex Inc.*, 550 U. S. 1, 15 (2007).

Appellants respectfully submit that the pending claims are patentable over the cited references for at least the reasons that the present rejection fails to teach or suggest all of the limitations of the claims nor does it provide the requisite suggestion or incentive that one of ordinary skill in the art would have to have had to combine the cited references in order to achieve the compositions and methods of the present invention exactly as claimed. Further, even if combined, the proposed modification/combination fails to provide a reasonable expectation of success in achieving the claimed invention. Thus, the Examiner has failed to make a *prima facie* case of obviousness.

The genome of the SARS coronavirus is approximately 29,700 bases in length. Laue discloses a 300 nucleotide sequence of the SARS genome and from this sequence provides particular primer pairs for detection of SARS using PCR. However, Laue fails to teach or suggest the specific primer pairs of the presently claimed invention. Further, the secondary reference, Lowe et al., fails to remedy the deficiencies of Laue.

Lowe et al. provides a program for finding, in a selected sequence, those sequences that fulfill the criteria designated by the user for the desired primers. The Office Action asserts that Lowe et al. would select primers for PCR from a known sequence. However, the Lowe et al. program is not sufficient for identifying useful SARS coronavirus primers as defined by the claimed invention, for at least the reason that after selecting the target sequence, the ordinary skilled person using the program must still single out and select the presently claimed pairs of primers from the large number of possible primers produced by the program. As noted above, the SARS coronavirus genome is over 29,750 bases in length; thus, the potential number of different primers and primer pair combinations would be exceedingly large. Even inputting the 300 bases of the nucleotide sequence of Laue would result in an extremely large population of primers, with no direction provided in how to select among the primers and how to select for specific primer pairs. Nothing in the cited art teaches or suggests or provides any direction for selecting the specific primer pairs of the present invention.

Thus, the cited references fail to teach or suggest the specific primers of the presently claimed invention, they fail to provide the motivation to combine the cited references in order to achieve the presently claimed invention and even if combined the cited references fail to provide a reasonable expectation of success in achieving the presently claimed invention.

Accordingly, applicants submit that claims 1-4, 11-14, and 16-18 are patentable over Laue in view of Lowe et al., and respectfully request the withdrawal of this rejection.

B. The Office Action states that claims 5 and 6 are rejected under 35 U.S.C. §103 for allegedly being unpatentable over Ahn et al. (Korean Patent Application No. 10-2003-0034331) in view of Lowe et al. and Laue. Specifically, the Office Action states that Ahn et al. discloses a nucleic acid sequence from SARS virus which comprises instant SEQ ID NOs:14 and 17. The Office Action further states that one of ordinary skill in the art would have been motivated to construct a pair of oligonucleotides within instant SEQ ID NOs:14 and 17 for amplifying a target sequence encoding the nucleocapsid protein of SARS coronavirus with reasonable expectation of

success because Ahn et al. discloses a known nucleic acid sequence, Laue discloses a method of detecting SARS with a pair of primers and Lowe et al discloses a computer program for selecting oligonucleotide primers from PCR from a known sequence. On this basis the Office Action concludes that it would have been *prima facie* obvious to construct a pair of oligonucleotides from within the instant SEQ ID NOs:14 and 17 for amplifying a target sequence of the genome of SARS coronavirus. Applicants respectfully traverse this rejection.

As mentioned above, the genome of the SARS coronavirus is approximately 29,700 bases in length. Ahn et al. discloses a 520 nucleotide sequence of the SARS genome. However, Ahn et al. fails to teach or suggest the specific primer pairs as claimed in the present invention, i.e., the nucleotide sequence of SEQ ID NO:14 and the nucleotide sequence of SEQ ID NO:17. Further, Lowe et al. and Laue, fail to remedy the deficiencies of Ahn et al.

As discussed above, Lowe et al. provides a program for finding, in a pre-selected sequence, those sequences that fulfill the criteria designated by the user for the desired primers. The Office Action asserts that Lowe et al. would select primers for PCR from a known sequence. However, the Lowe et al. program is not sufficient for identifying useful SARS coronavirus primers, as defined by the claimed invention, for at least the reason that after selecting the target sequence, the ordinary skilled person using the program must still single out and select the presently claimed pairs of primers from the vast number of possible primers produced by the program. As noted above, the SARS coronavirus genome is over 29,750 bases in length; thus, the potential number of different primers and primer pair combinations would be exceedingly large. Even inputting the 520 bases of the nucleotide sequence of Ahn et al. would result in an extremely large population of primers, with no direction provided in how to select among the primers or how to select for any specific primer pairs. Nothing in the cited art teaches or suggests or provides any guidance in selecting the specific primer pairs of the present invention.

Laue discloses a 300 nucleotide sequence of the SARS genome and from this sequence provides particular primer pairs for detection of SARS using PCR. However, similar to Ahn et

al., Laue fails to teach or suggest the specific primer pairs of the presently claimed invention.

Thus, the cited references fail to teach or suggest or provide any direction to produce the specific primers of the presently claimed invention, they fail to provide the motivation to combine the cited references in order to achieve the presently claimed invention and even if combined the cited references fail to provide a reasonable expectation of success in achieving the presently claimed invention.

Accordingly, applicants submit that claims 5 and 6 are patentable over Ahn et al. in view of Lowe et al. and Laue and respectfully request the withdrawal of this rejection.

C. The Office Action states that claims 7-10 are rejected under 35 U.S.C. §103 for allegedly being unpatentable over Briese et al. (U.S. Patent Application Publication No 20040265796) in view of Lowe et al. Specifically, the Office Action alleges that SEQ ID NO:1 of Briese et al. comprises instant SEQ ID NOs:23, 26 and 34 and that Figure 1 of Briese et al. comprises instant SEQ ID NO:31 of the presently claimed invention. The Office Action further states that one of ordinary skill in the art would have been motivated to construct a pair of oligonucleotides within the gene encoding the nucleocapsid protein of the genome of SARS coronavirus with a reasonable expectation of success because Briese et al. discloses an assay of detecting SARS with a pair of primers from a known sequence and Lowe et al. discloses a computer program for selecting oligonucleotide primers for PCR from a known sequence. On this basis, the Examiner concludes that it would have been *prima facie* obvious to construct a pair of oligonucleotides within SEQ ID NOs:23, 26, 31, and 34 for amplifying a target sequence located within the gene encoding the nucleocapsid protein of the genome of SARS coronavirus. Applicants respectfully traverse this rejection.

SEQ ID NO:1 of Briese et al. discloses a sequence of 1136 nucleotides from the SARS genome. Figure 1 of Briese et al. discloses the SARS-associated coronavirus genome, which is over 29,700 bases in length. Briese et al. fails to identify or suggest the specific primers and

primer pairs as claimed in the present invention, i.e., SEQ ID NO:23, SEQ ID NO:26, SEQ ID NO:34 and SEQ ID NO:31 from among the 1136 nucleotides disclosed in SEQ ID NO:1 of Briese et al. or from the entire genome of the SARS-associated coronavirus as disclosed in Figure 1 of Briese et al. Further, the secondary reference, Lowe et al., fails to remedy the deficiencies of Briese et al.

As discussed above, Lowe et al. provides a program for finding, in a pre-selected sequence, those sequences that fulfill the criteria designated by the user for the desired primers. The Office Action asserts that Lowe et al. would select primers for PCR from a known sequence. However, the Lowe et al. program is not sufficient for identifying useful SARS coronavirus primers, as defined by the claimed invention, for at least the reason that after selecting the target sequence, the ordinary skilled person using the program must still single out and select the presently claimed pairs of primers from the vast number of possible primers produced by the program. Inputting the 1136 bases of the nucleotide sequence of SEQ ID NO:1 of Briese et al. or the entire genome of the SARS coronavirus as presented in Figure 1 of Briese et al. would result in an exceedingly large population of primers, with no direction provided in Briese et al. as to how to select among the primers or for specific primer pairs.

Thus, the cited references fail to teach or suggest or provide any direction to produce the specific primers of the presently claimed invention, they fail to provide the motivation to combine the cited references in order to achieve the presently claimed invention and even if combined the cited references fail to provide a reasonable expectation of success in achieving the presently claimed invention.

Accordingly, applicants submit that claims 7-10 are patentable over Briese et al. in view of Lowe et al. and respectfully request the withdrawal of this rejection.

D. The Office Action states that claim 15 is rejected under 35 U.S.C. §103 for allegedly being unpatentable over Laue in view of Lowe et al. in further view of Tyagi (*Nature Biotechnol.* 14:303-308 (1996)). Specifically, the Office Action states that one of ordinary skill in the art

would have been motivated to apply a molecular beacon probe for detection as taught by Tyagi et al. and that it would have been *prima facie* obvious to apply a molecular beacon probe for detection.

For the reasons discussed above, applicants submit that Laue and Lowe et al., alone or in combination, fail to disclose or suggest the primers and primer pairs of the presently claimed invention. Further, Tyagi et al. fails to remedy the deficiencies of Laue and Lowe et al. Tyagi et al. simply discloses the use of molecular beacon probes generally, but similar to Laue and Lowe et al., Tyagi et al. fails to teach or suggest the specific primers and primer pairs of the present invention, alone or in combination, with a molecular beacon probe.

Accordingly, applicants submit that claim 15 is patentable over Laue in view of Lowe et al. in further view of Tyagi and respectfully request the withdrawal of this rejection.

E. The Office Action states that claims 19-21 are rejected under 35 U.S.C. §103 for allegedly being unpatentable over Laue in view of Lowe et al. in further view of Compton et al. (*Nature* 350:91-92 (1991)). Specifically, the Office Action states that one of ordinary skill in the art would have been motivated to apply a NASBA reaction for detection of SARS nucleic acid in a sample and that it would have been *prima facie* obvious to carry out a NASBA reaction and to make a kit including a NASBA reagent for detecting SARS nucleic acid in a sample.

For the reasons discussed above, applicants submit that Laue and Lowe et al., alone or in combination, fail to disclose or suggest the primers and primer pairs of the presently claimed invention. Further, Compton fails to remedy the deficiencies of Laue and Lowe et al. Compton discloses the use of a standard NASBA reaction, but similar to Laue and Lowe et al., Compton et al. fails to teach or suggest the specific primers and primer pairs of the present invention and thus, fails to teach or suggest their use in a NASBA reaction.

Accordingly, applicants submit that claims 19-21 are patentable over Laue in view of Lowe et al. in further view of Compton et al. and respectfully request the withdrawal of this

rejection.

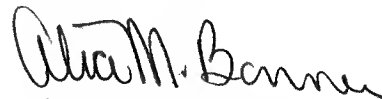
II. New Claim 22.

New claim 22 recites the pair of oligonucleotides according to claim 1, wherein each oligonucleotide is 18-26 nucleotides in length and comprises at least 20 contiguous nucleotides. Support for this new claim can be found in the language of the original claims and throughout the specification, for example, at least, in original claim 13. This claim is believed to be patentable over the cited art for the same reasons set forth above regarding claims 1-21.

Having addressed all of the issues raised by the Examiner in the present Office Action, Applicants believe that the present application is in condition for allowance, which action is respectfully requested. The Examiner is encouraged and invited to contact the undersigned directly if such contact will expedite the prosecution of the pending claims to issue.

No fee is believed due with this response. However, the Commissioner is authorized to charge any deficiency or credit any overpayment to Deposit Account No. 50-0220.

Respectfully submitted,



Alice M. Bonnen

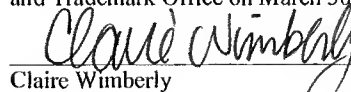
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Claire Wimberly